UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/813,760	03/31/2004	Joel E. Bernstein	41959-102739	5267

23644 7590 10/05/2009

BARNES & THORNBURG LLP
P.O. BOX 2786
CHICAGO, IL 60690-2786

EXAMINER	
KWON, BRIAN YONG S	
ART UNIT	PAPER NUMBER
1614	
NOTIFICATION DATE	DELIVERY MODE
10/05/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Patent-ch@btlaw.com

Advisory Action Before the Filing of an Appeal Brief	Application No.	Applicant(s)	
	10/813,760	BERNSTEIN, JOEL E.	
	Examiner	Art Unit	
	Brian-Yong S. Kwon	1614	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 06 August 2009 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).

5. ☐ Applicant's reply has overcome the following rejection(s): _____.

6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1-3,5-9 and 11-15*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).

9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).

10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See below or attached.

12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____

13. ☐ Other: _____.

/Brian-Yong S Kwon/
Primary Examiner, Art Unit 1614

For the reason of record. In response to applicant's argument that the examiner neither refuted nor responded to the teaching of Kroger et al. 1999 publication, the examiner likes to point out that applicant has received an action on the merits for the originally elected invention, an acetaminophen as the hepatotixc compound. Accordingly the search and examination have been only extended to an acetaminophen alone in combination with methionine and nicotinmaide. Contrary to the merits of the case, Kroger'99 reference discussed the activity of methionine and/or nicotinamide in reducing essentially the liver toxicity of methotrexate. Although acetaminophen is disclosed in the toxicity study, a lower dose (50mg/kg) utilized in the study is not known to cause hepatotoxicity as seen in the Table 3 (as well as line 3 of the abstract). There is no conclusive evidence indicated in Kroger'99 that nicotinamide is non-hepatoprotective at high dosage and at lower dosage nicotinamide increases liver damage from acetaminophen. As discussed in preceding comments, the examiner's search and examination have not been extended beyond acetaminiphen. Thus, the examiner has not (fully) considered Kroger'99 reference since it is premature to discuss about non-elected species, methotrexate. Even assuming arguendo that Kroger'99 is relevant to the merits of the case, Table 5 discloses that with increasing NA doses, there is a reduction in GOT and GPT activities. Thus, coupled with the result of Table 4, one having ordinary skill in the art would have perceived that the simultaneous administration of either nicotinamide or methionine or both together would be useful in reducing the liver toxic effect of methotrexate, more broadly other drugs at doses known to be hepatotoxic, e.g., acetaminophen (see last ten lines in column 2 of page 205, under "Discussion" of Kroger'99)